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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,660	02/08/2006	Suzanne Chamberland	4810-73194-01	3960

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/567,660	CHAMBERLAND ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2-8-06 (Pre. Amdt)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6,7,9-12,18-25,29,31 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,7,9-12,18-21,29,31 and 39* is/are rejected.

7)☒ Claim(s) *22-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/06 + 2/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

NON-FINAL ACTION

Applicant's preliminary amendment of 2-8-06 is acknowledged.

Claims 3, 5, 8, 13-17, 26-28, 30, 32-38 and 40-42 are cancelled.

Claims 1, 2, 4, 6, 7, 9-12, 18-25, 29, 31 and 39 are pending.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1, 2, 4, 6, 7, 9-12, 18-21, 29, 31 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1 recites the limitation of "*solubilizing group*" which has indefinite metes and bounds because it is not clear what moieties constitute such a group. The specification only cites a few examples of a "*solubilizing group*", but definition is open-ended, and thus it is not clear as to what other groups would be considered a "*solubilizing group*".

b. The definition of R_1 includes C_1-alkenyl and C_1-alkynyl, which does not make sense because said groups require at least two carbon atoms.

c. Claim 9 recites the limitation of "amine containing heterocycle" which is not clear. Is an amine present as a substituent or as a ring member. Furthermore, what type of atoms are permitted as ring members. Note, **In re Wiggins 179 USPQ 421**.

d. The scope of "substituted" aryl for R_2 is unclear. As defined in the specification (page 8), it includes open-ended and incomplete moieties such as phosphoryl, phosphonate, carbonyl, thiocarbonyl as well as classes of compounds (e.g., ketones, esters, etc.) whose structural makeup is not set forth much less point of attachment. Additionally, exacerbating the scope is the presence of additional classes of compounds included as substituents on the substituents.

e. Several dependent claims (10, 12 and 19) recite compounds per se which have no free valency. Thus, their attachment to remainder of molecule is not known. See, N-methylpiperazine, hydroxyethanol, hydroxyaniline, 4-hydroxyaniline, N-alkylimidazole.

f. Species in claims 20 and 21 are incomplete as written. Are they cis- or trans-? Note, definition of "X" in claim 1.

g. Claim 39 recites a process with optional steps which makes it unclear what the required starting materials are needed to react with formula (1.7).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 1, 2, 4, 6, 7, 9-12, 18,19, 29, 31 and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using compounds wherein R_1 or R_2 is *phenyl*, or *hydroxyphenyl*, does not reasonably provide enablement for making and using compounds wherein R_1 or R_2 is another ring embraced in the definition of "**aryl**" or "substituted" derivatives recited for R_2 which is virtually non-limiting for many of the moieties described in specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claim 1 recites a quinazoline formula in which R_1 and R_2 can be an "*aryl*" group. The scope of "*aryl*" covers an extensive list of rings including many heteroraryl rings as well, see the following excerpt:

> **[0025] The term "aryl" refers to aromatic radicals having 3-14 ring atoms and at least one ring having a conjugated pi electron system. Preferably at least two, more preferably at least four, of the ring atoms are carbon atoms. For example aryl may be a C_5, C_6, C_7, C_8, C_9 or C_{10} ring. The term "aryl" encompasses "heteroaryl" compounds. The term "heteroaryl" refers to an aromatic heterocyclic group usually with one or more heteroatoms selected from O, S and N in the ring. Examples of aryl include without limitation phenyl, substituted phenyl, pyridyl, substituted pyridyl, pyridinyl, substituted pyridinyl, thiophenyl, substituted thiophenyl, furanyl, substituted furanyl, thiazole, oxazole or substituted or unsubstituted imidazole. Such substituents can include,**

Thus, the scope of R_1 and R_2 is extensive which renders the scope of claims 1 and dependents thereon unduly broad.

The amount of direction or guidance presented: Only quinazoline compounds with R_1 or R_2 as a phenyl or hydroxyphenyl group are made and tested for antibacterial property. The specification is silent as to the availability of necessary reactants needed to prepare a quinazoline compound with R_1 or R_2 as a heteroaryl moieties. Note, **In re Howarth** 210 USPQ 689; **Ex parte Moersch** 104 USPQ 122, for the need to show starting material sources commensurate with the claims' scope.

Regarding the biological activity, the antibacterial property of the tested compounds cannot be extrapolated to other compounds wherein R_1 or R_2 is other than *phenyl* as there is no evidence of recognized biological equivalency for such diverse groups.

Thus, the specification does not provide sufficient enablement commensurate with the broad Markush group claimed herein.

The state of the prior art: Although the state of the art as evident by **Hermann** (DE'280 cited on IDS) allows for a heterocyclic group at the 4-position on the quinazoline, such a group is saturated (or non-aromatic). Due to non-aromaticity, the antimicrobial property of Hermann's compounds cannot be extrapolated to those claimed herein with R_1 or R_2 as a heteroaryl group. Thus, the state of the art does not support the entire compound scope of claim 1 and dependents thereon.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to carry out extensive research to select an effective compound from the claimed Markush group. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index and pharmacokinetic profile for each compound. Given a Markush group as claimed herein, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case the limited number of tested compounds with R_1 or R_2 as a phenyl group does not sufficiently determine the antibacterial property for compounds in which R_1 or R_2 is another ring.

Note, the "how to use" requirements of 35 USC 112 are not met by disclosing only a pharmacological activity of the claimed compound if one skilled in the art would not be able to use the compound effectively without undue experimentation. See **In re Diedrich**, 138 USPQ 128; **In re Gardner et. al.**, 166 USPQ 138. Thus, where claimed compounds do not bear structures that are similar to known compounds having the same activity and their pharmaceutical properties could not be predicted from their chemical structure, a disclosure that they possess a particular activity may not suffice as a description of how to use as required by 35 USC 112. Thus, given the unpredictable nature of the art, and the vast number of compounds claimed herein, one skilled in the art will have to carry out undue experimentation to practice the method of treatment recited in claims 1, 2, 4, 6, 7, 9-12, 18,19, 29, 31 and 39.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 4, 11, 29, 31 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by **Hermann et. al.** (DE 2,140,280 or DE'280). On page 9, Hermann et. al. disclose compound #16 which reads on the instant formula with the following substituents:

i. R_1 is an alkyl group;

ii. R_2 is hydrogen;

iii. R_3 is hydrogen;

iv. R_4 is halogen;

v. X is CHCH.

The compound has antimicrobial or antibacterial property, and thus, the instant method claims 29 and 31 are also anticipated.

Page 4 of DE'280 outlines the process of making such a compound which corresponds to the instant claim 39 (step d).

Claim Objections

4. Claims12, 18 and 22-25 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

a. Claim 12 recites "hydroxyaniline" and "4-hydroxyaniline" for R_1 which suggests an additiona NH_2 group on the phenyl ring which is not further limiting claim 1.

b. Claims 22 and 23 recite species having chloro at the 4-position which are not within the genus of formula (1.0).

c. Claims 24 and 25 recite species having no group corresponding to $-NR_1R_2$ of formula (1.0).

d. Claim 18 recites "pyranyl" which is not an aromatic ring, and thus outside the scope of "aryl" as defined in specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Tamthom N. Truong
Examiner
Art Unit 1624

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5-11-07

EMILY BERNHARDT
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GROUP 1600